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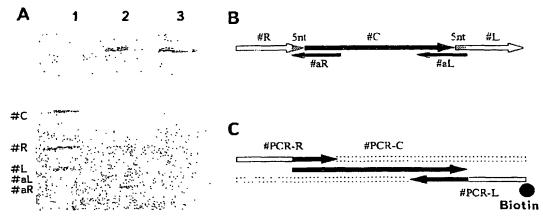
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#### (54) Title: LIGATION-BASED SYNTHESIS OF OLIGONUCLEOTIDES WITH BLOCK STRUCTURE



(57) Abstract: The present invention relates to a method of producing single-stranded nucleic acid molecules from oligo- or polynucleotides wherein each of said oligo- or polynucleotides has a predefined 5' or 3' terminus, comprising the steps of (a) annealing an adaptor oligonucleotide simultaneously or step by step to (aa) a first oligo- or polynucleotide; and (ab) a second oligo- or polynucleotide wherein the 5'-terminus of said adaptor oligonucleotide is complementary in sequence to the 5' terminus of said first oligo- or polynucleotide and the 3'terminus of said adaptor molecule is complementary in sequence to the 3' terminus of said second oligo- or polynucleotide; and optionally (a') simultaneously with or subsequently to step (a) annealing at least one further adaptor oligonucleotide to free termini of said first or second oligonucleotides and to free termini of further oligo- or polynucleotides; (b) optionally filling in gaps between the neighbouring ends of said oligo- or polynucleotides; (c) ligating said oligo- or polynucleotides; and (d) removing said at least one adaptor oligonucleotide. In a preferred embodiment of the method of the invention, said single-stranded nucleic acid molecules represent a collection of nucleic acid molecules wherein either said first or said second oligo- or polynucleotide is invariable in sequence between all members of said collection of nucleic acid molecules.



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## INTERNATIONAL SEARCH REPORT

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CLASSIFICATION OF SUBJECT MATTER
PC 7 C12N15/10 C12N15/66 C12P19/34 C1201/68 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N C12P C12Q Documentation searched other than minimum documentation to the extent that such documents are included. In the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS, WPI Data, PAJ, CAB Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Category ° Citation of document, with indication, where appropriate, of the relevant passages 1-4,10, "A NEW METHOD FOR THE HAI-BAO CHEN ET AL: SYNTHESIS OF A STRUCTURAL GENE" 15,16 NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 18, no. 4, 25 February 1990 (1990-02-25), pages 871-878, XP000099685 ISSN: 0305-1048 figure 1 WO 97/42330 A (APOLLON INC) 1-4,10, X 13 November 1997 (1997-11-13) 22 page 7, line 19 - page 9, line 36; figures 1-4,10, X WO 00/29616 A (PERKIN ELMER CORP) 25 May 2000 (2000-05-25) 15,16 claims 1-22; figures 1-6 Patent family members are listed in annex. Further documents are listed in the continuation of box C. X Special categories of cited documents: \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "A" document defining the general state of the art which is not considered to be of particular relevance \*E\* earlier document but published on or after the International "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of enother citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or other means ments, such combination being obvious to a person skilled document published prior to the international filing date but later than the priority date claimed \*&\* document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 26 October 2004 08/11/2004 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

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